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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,879	05/22/2001	Kazuya Katagai	MUR-026-USA-	8324

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EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,879	KATAGAI ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,11-13 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,11-13 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Request for Continued Examination received December 2, 2004 is acknowledged. Claims **1, 8, 11-12, and 17** are pending in this application. Claims 2-7, 9-10, and 14-16 stand cancelled. Claim 13 is withdrawn as being directed to a non-elected invention.

Specification

The objection of the amendment to the specification for introducing new matter is withdrawn.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 3, 5-12, 14, and 17 under 35 U.S.C. 112, first paragraph, based on new matter is withdrawn.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 3, and 14 under 35 U.S.C. 102(b) as being anticipated by WO 96/24352 is withdrawn in view of the amendment of 12/27/04 specifying the drug, lidocaine and epinephrine and the acidic polymer, polyacrylic acid.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 8, 11-13, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 1 recites: An adhesive gel composition comprising: a) lidocaine and epinephrine, b) polyacrylic acid, c) a polyfunctional epoxy compound, d) water, e) a polyhydric

alcohol **and/or** f) a gelatin, g) an antioxidant. This claim is indefinite and vague since it is unclear what the limitation of "and/or" is. For instance, is the and/or referring to a composition that can have a polyhydric alcohol and/or component (f) and (g)? Or is the and/or referring to a composition that can have a polyhydric alcohol or gelatin or both? Further clarification is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 8, 11-12, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oda et al (5,725,874) in view of Linkwitz et al (6,295,469).

Oda et al teach an external preparation that contains a) 0.001-20% of a drug such as instant lidocaine, b) 1-30% of one or more water-soluble polymer in the amount of 1-30% such as polyacrylic acid, isobutylenemaleic anhydride copolymer, polyvinylpyrrolidones, polyvinyl alcohol, sodium carboxymethyl cellulose, and gelatin, c) a polyfunctional epoxy compound d)

water, e) polyhydric alcohol. See column 3. The base may include a crosslinking agent such as a polyfunctional epoxy compound. See column 4, lines 13-30. The preferable amount of drug is 0.001-20 and more preferably 0.5-10% and the water-soluble polymer in the amount of 1-30%, preference to 1-20%, and ideally 1-15%. Further, antioxidants such as ascorbic acid, tocopherol, etc. are taught. See column 4, lines 35-40. Various drug: polymer ratios including the instant range are utilized in the examples.

Oda does not teach the instant lidocaine and epinephrine combination.

Linkwitz et al teach a formulation for electrically assisted delivery of lidocaine and epinephrine. Linkwitz teaches the presence of epinephrine helps retard adsorption of lidocaine, thereby reducing its systemic toxicity. Epinephrine also increases the duration of the drug's local anesthetic effect. The vasoconstrictive effect of epinephrine maintains localization of lidocaine a the nerve, thereby prolonging the effect of action of lidocaine. See column 1, lines 40-55. Lidocaine is utilized in the amount of 1-10% and about 0.01-0.2% epinephrine. See column 3, lines 20-28. Further, Linkwitz teaches that epinephrine is degraded by oxygen and reduces the storage ability of lidocaine. To enhance the stability, the reference teaches the use of antioxidants such as sodium metabisulfite in the amount of 0.01-0.2%. See column 4, lines 20-35. Further, the reference teaches the use of hydrophilic polymers for the drug matrix. Suitable polymers include polyvinylpyrrolidones, polyvinyl alcohol, sodium carboxymethyl cellulose, Carbopol (polyacrylic acid), etc.. See column 4.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Oda and Linkwitz et al and utilize the instant active agents in Oda's formulation. One would have been motivated to do so since Linkwitz teaches that

epinephrine provides prolonged effect of an analgesic such as instant lidocaine, for transdermal administration. Thus, it is prima facie obvious to combine the instant lidocaine with instant epinephrine to prolong the effect of the analgesic, i.e. lidocaine.

With regard to the instant antioxidant, sodium hydrogen sulfite and Linkwitz's antioxidant sodium metabisulfite are obvious substitutions of each other.

Claims 1, 8, 12, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oda et al (5,725,874) in view of Lugnani et al (5,843,016).

Oda et al teach an external preparation that contains a) 0.001-20% of a drug such as instant lidocaine, b) 1-30% of one or more water-soluble polymer in the amount of 1-30% such as polyacrylic acid, isobutylenemaleic anhydride copolymer, polyvinylpyrrolidones, polyvinyl alcohol, sodium carboxymethyl cellulose, and gelatin, c) a polyfunctional epoxy compound d) water, e) polyhydric alcohol. See column 3. The base may include a crosslinking agent such as a polyfunctional epoxy compound. See column 4, lines 13-30. The preferable amount of drug is 0.001-20 and more preferably 0.5-10% and the water-soluble polymer in the amount of 1-30%, preference to 1-20%, and ideally 1-15%. Further, antioxidants such as ascorbic acid, tocopherol, etc. are taught. See column 4, lines 35-40. Various drug: polymer ratios including the instant range are utilized in the examples.

Oda does not teach the instant lidocaine and epinephrine combination.

Lugnani et al teach a method of treating acute urinary obstruction utilizing electromotive (transdermal) drug administration. See abstract. The reference teaches the use of various drugs for transdermals such as analgesic drugs, i.e. lidocaine, mepivacaine, bupivacine, and ropivacaine in the amount of 0.3-1%. Furthermore, Lugnani teaches the use of the analgesics

with epinephrine in a concentration of 1/200000-1/50000 in order to achieve a prolonged effect. See column 11, lines 49-56.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Oda et al and Lugnani et al and utilize the instant active agents in Oda's formulation. One would have been motivated to do so since Lugnani teaches that epinephrine provides prolonged effect of an analgesic such as instant lidocaine. Therefore, it is prima facie obvious to combine the instant lidocaine with epinephrine to prolong the effect of the analgesic. Further, one would expect similar results since both references provide for transdermal administration of the active agents and Lugnani establishes the state of the art wherein it is known in the art to utilize the instant combination.

Response to Arguments

Applicant argues that Oda et al fails to disclose the instant amendments. Applicant argues that both the reference Lugnani and Linkwitz cannot be used as prior art since both have issue dates after the instant priority date.

Applicant's argument have been fully considered but they are not persuasive. Firstly, the examiner points out that Oda teaches a) 0.001-20% of a drug such as instant lidocaine, b) 1-30% of one or more water-soluble polymer in the amount of 1-30% such as polyacrylic acid, isobutylenemaleic anhydride copolymer, polyvinylpyrrolidones, polyvinyl alcohol, sodium carboxymethyl cellulose, and gelatin, c) a polyfunctional epoxy compound d) water, e) polyhydric alcohol. With regard to the instant ratio, the examiner points out that the examples utilize the instant ratio. The only element missing is the use of lidocaine and epinephrine. Thus, the examiner relies on the secondary references to cure this deficiency.

With regard to the secondary references, the examiner points out that Linkwitz has a filing date of 11/14/97 which qualifies as a 102(e) reference and it is prior to applicant's priority date of 11/26/98. Lugnani has a filing date of 3/18/96 which also qualifies as a 102(e) reference and it is prior to applicant's priority date of 11/26/98. Thus, the secondary references qualify as prior art references.

Claims 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oda et al (5,725,874) in view of Lugnani et al (5,843,016) in further view of JP 08-325149.

As set forth above, Oda et al teach an external preparation that contains a) 0.001-20% of a drug such as instant lidocaine, b) 1-30% of one or more water-soluble polymer in the amount of 1-30% such as polyacrylic acid, isobutylenemaleic anhydride copolymer, polyvinylpyrrolidones, polyvinyl alcohol, sodium carboxymethyl cellulose, and gelatin, c) a polyfunctional epoxy compound d) water, e) polyhydric alcohol. See column 3. Further, antioxidants such as ascorbic acid, tocopherol, etc. are taught. See column 4, lines 35-40.

The reference do not specify the instant antioxidant.

JP teaches an external preparation containing an active agent (pridinol), water-soluble polymers (polyacrylic acid polymer), polyhydric alcohols (glycerol/ benzyl alcohol blend), and antioxidant (sodium hydrogen sulfite). Crosslinking agents such as organic acid or salt of an organic acid are included in the composition. See Detailed Description in its entirety). JP teaches a stabilizing agent such as instant sodium hydrogen sulfite, L-ascorbic acid, tocopherol, , BHT, etc. see page 8.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the teachings of JP 08-325149 and incorporate its teaching into Oda and

utilize the instant antioxidant. One would have been motivated to do so since JP teaches the functional equivalency of the instant antioxidant and Oda's antioxidants. Therefore, it is prima facie obvious to substitute an equivalent antioxidant for the prior art's antioxidant with the expectation of similar results since the prior art establishes functional equivalency.

Conclusion

None of the claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG

Gary L. Kunz

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